

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re the Application of: **Shigeru KANAOKA**

Art Unit: 1637

Application Number: **10/549,389**

Examiner: **Christopher M Babic**

Filed: **September 14, 2005**

Confirmation Number: **2212**

For: **METHOD OF DETECTING COLON CANCER MARKER**

Attorney Docket Number: **091228**

Customer Number: **38834**

**DECLARATION UNDER 37 C.F.R. §1.132**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Shigeru Kanaoka, a citizen of Japan, hereby declare and state the following:

1. I graduated from Hamamatsu University School of Medicine of Hamamatsu, Shizuoka, Japan in 1987 with an M.D. degree. In 1997, I was awarded a Ph.D. in gastroenterology for my work on colon carcinogenesis

2. Since 1987, I have been employed by Hamamatsu University. During my employment therein, I have conducted clinical research in gastroenterology and basic research in gastrointestinal oncology. Since 2000, I have been an assistant professor in the First Department of Medicine. Since 2007, I have been a professor in the Department of Molecular Diagnosis.

3. I have read and am familiar with the above-identified patent application as well as the Official Action dated February 25, 2010, in the application.

4. Under my supervision and control, I conducted experiments to obtain data relating to COX-2 expression in colon cancer patients and non-colon cancer patients. This data was

previously submitted in the application as originally filed. Additional data was submitted with the Declaration filed April 27, 2009.

7. Based on the previously submitted "raw data," the following summary and calculations have been prepared in accordance with typical epidemiological practice.

**Data from Specification (from page 9, lines 23-28):**

There are 30 cancer patients. 27 of them had COX-2 expression

There are 22 healthy patients. 0 of them had COX-2 expression.

	With disease	Without disease	Total
<b>Positive test result</b>	27 (true positives)	0 (false positives)	27 (total positives)
<b>Negative test result</b>	3 (false negatives)	22 (true negatives)	25 (total negatives)
<b>Total</b>	30 (total diseased)	22 (total healthy)	52 (all tested)

Sensitivity = True positive / (true positive + false negative)  
= 27 / (27 + 3)  
= 27 / 30  
= 90% Sensitivity

Specificity = True negative / (true negative + false positive)  
= 22 / (22 + 0)  
= 22 / 22  
= 100% Specificity

Prevalence = total diseased / all tested  
= 30 / 52  
= 57.6% prevalence

Positive Predictive Value = true positives / total positives  
= 27 / 27  
= 100%

Negative Predictive Value = true negatives / total negatives  
= 22 / 25  
= 88%

**Data from Declaration (from Declaration filed April 27, 2009):**  
There are 70 cancer patients. 60 of them had COX-2 expression  
There are 34 healthy patients. 0 of them had COX-2 expression.

	With disease	Without disease	Total
Positive test result	60 (true positives)	0 (false positives)	60 (total positives)
Negative test result	10 (false negatives)	34 (true negatives)	44 (total negatives)
Total	70 (total diseased)	34 (total healthy)	104 (all tested)

Sensitivity = True positive / (true positive + false negative)  
=  $60 / (60 + 0)$   
=  $60 / 60$   
= 100% Sensitivity

Specificity = True negative / (true negative + false positive)  
=  $34 / (34 + 0)$   
=  $34 / 34$   
= 100% Specificity

Prevalence = total diseased / all tested  
=  $70 / 104$   
= 67.3% prevalence

Positive Predictive Value = true positives / total positives  
=  $60 / 60$   
= 100%

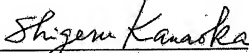
Negative Predictive Value = true negatives / total negatives  
=  $34 / 44$   
= 77%

8. From the attached experimental results and statistical analysis, I have concluded, among other things, that colon cancer can be reliably and predictably detected based on the observed expression of COX-2.

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Declaration under 37 C.F.R. §1.132  
Attorney Docket No.: 091228

The undersigned declares that all statements made herein of his own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application or any patent issued thereon.

  
Shigeru Kanaoka

Signed this 11 day of May, 2010.